The Egyptian Journal of Hospital Medicine (July 2025) Vol. 100, Page 4339-4344

Culture Negative Left Sided Endocarditis and Immune Mediated Acute Kidney Injury Following Covid 19 in Previously Healthy Sixteen-Month-Old Female Child

Abdelaziz Abd El-Atty Mahmoud [1,2]*, Ahmed Abd Elhakim Kamara [2], Mohamed Hussien Ghozlan [2], Ayman Mohamed Badr[1], Mohamed Ibrahem Ismaiel [1,2], Hany Risk Saad [2], Karem Ghalab [2], Ahmed Mamdouh Abdelaziz [2]

[1] Pediatric Cardiology Department, [2] Pediatric Intensive Care Department,
El Behera Specialized Pediatric Hospital, Abou Homos, Behera, Egypt

*** Corresponding author:** Abdel Aziz Abdel Atty Mahmoud**, Email:** abdalazizabobahia@gmail.com, **Phone:** +201225811314

ABSTRACT

Background: Infective endocarditis (IE) in children is rare, particularly in those without congenital heart disease or chronic comorbidities. Post–COVID-19 immune dysregulation has emerged as a potential contributor to unusual cardiovascular complications. **Case Presentation:** We report a 16-month-old previously healthy female child presenting with recurrent fever, respiratory distress, and hypoxemia. Initial imaging revealed pulmonary edema and hemorrhage. Echocardiography demonstrated a mitral valve vegetation with moderate regurgitation, and a diagnosis of IE was made despite persistently negative blood cultures. Her course was complicated by acute kidney injury due to immune complex–mediated glomerulonephritis, requiring peritoneal dialysis, and by an embolic ischemic stroke confirmed on MRI. Inflammatory and thrombotic markers were markedly elevated, consistent with post–COVID-19 immune activation. Despite optimal medical therapy, the vegetation enlarged with progression to severe mitral regurgitation. Surgical removal of the vegetation and mitral valve repair were performed successfully, with subsequent clinical stabilization.

Conclusion: This case highlights culture-negative IE in a previously healthy child in the setting of post–COVID-19 immune dysregulation. Early recognition of complications, multidisciplinary management, and timely surgical intervention were crucial for a favourable outcome.

Keywords: Infective endocarditis, Pediatric, COVID-19, Culture-negative, Glomerulonephritis.

INTRODUCTION

Infective endocarditis (IE) is an uncommon but life-threatening condition in children, with an estimated incidence of only 0.43–0.69 cases per 100,000 children per year[1,2]. Compared with adults, pediatric IE has distinctive epidemiological and clinical features, most notably the predominance of congenital heart disease (CHD) as the leading predisposing factor[3]. The overall incidence in childhood remains lower than in adulthood; however, recent decades have witnessed a relative rise, largely attributable to the increasing survival of children with congenital cardiac anomalies, the use of intravascular devices, and the growing population of immunocompromised patients[4, 5]. Although CHD, indwelling catheters, and chronic medical conditions constitute the major risk factors, a minority of cases occur in children without prior structural cardiac disease[6]. Approximately 8–10% of pediatric IE cases arise in this setting, often in association with alternative vulnerabilities such as immunodeficiency, prolonged parenteral nutrition, or the presence of central venous catheters[7]. These cases are clinically challenging, as the absence of known cardiac pathology may delay recognition and increase the risk of complications.

The coronavirus disease 2019 (COVID-19) pandemic has introduced additional cardiovascular concerns in pediatric populations. Beyond acute infection, SARS-CoV-2 has been implicated in triggering a prothrombotic and inflammatory milieu, leading to microvascular thrombosis, myocardial injury, and arrhythmias[8-10]. This hypercoagulable state, together with post-infectious immune dysregulation, may create a substrate for unusual cardiovascular manifestations, including conditions not traditionally linked to viral illness, such as IE.

Here, we reported a case of previously healthy 16-month-old female child who developed culture-negative IE complicated by immune-mediated glomerulonephritis and embolic stroke in the setting of recent COVID-19 infection.

The aim of this report is to highlight the potential role of post-COVID immune dysregulation in predisposing otherwise healthy children to severe endocardial infection and systemic complications, underscoring the importance of early recognition and multidisciplinary management.

CASE PRESENTATION

Initial Presentation

A 16-month-old previously healthy female child, weighing 12 kg, was brought to the emergency department with recurrent fever, respiratory distress, and poor oral intake. She had experienced an upper respiratory tract infection one week earlier that initially improved with antipyretics, but fever recurred with progressive dyspnea and refusal of feeds. There was no prior history of CHD, chronic illness, or immunodeficiency. Prenatal and perinatal history were unremarkable, and developmental milestones were appropriate for age. Family history was non-contributory.

Received: 29/04/2025
Accepted: 29/06/2025

Clinical Findings on Admission

On presentation, the child was alert but in distress, pale, and tachypneic (RR 65/min) with marked tachycardia (HR 190/min), febrile (38 °C), and hypoxemic (SpO_2 88% on room air). Chest examination revealed diffuse crepitations with subcostal retractions. Cardiovascular examination showed a capillary refill time of 2 seconds and a systolic murmur over the mitral area. Abdominal examination revealed tender hepatomegaly. Neurological assessment showed no focal deficits at that time.

Initial Investigations and Management

Chest radiography demonstrated bilateral pulmonary edema with features consistent with pulmonary hemorrhage **(Figure 1)**. ECG showed sinus tachycardia. Laboratory evaluation revealed anemia (hemoglobin 7.4 g/dL), elevated C-reactive protein (72 mg/L), and normal coagulation profile. Arterial blood gases confirmed respiratory acidosis (pH 7.20, PCO_2 66 mmHg). The patient was admitted to the pediatric intensive care unit (PICU), intubated, and placed on mechanical ventilation. Bloody secretions were noted from the endotracheal and orogastric tubes, favouring cardiogenic pulmonary hemorrhage over coagulopathy. She received diuretics, blood transfusion, and supportive care.

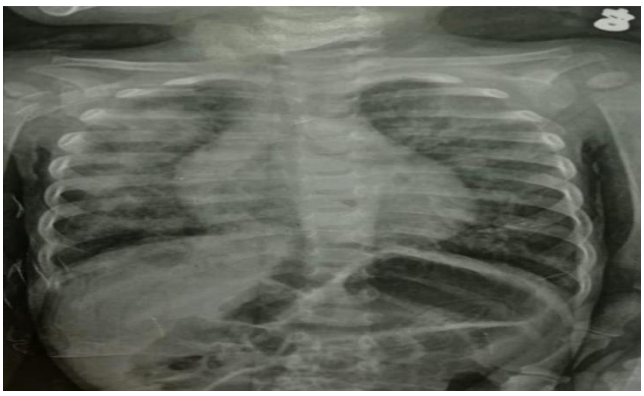

Figure 1: Chest X-ray (anteroposterior view) showing bilateral pulmonary hemorrhage.

Cardiac Assessment

Echocardiography revealed an intracardiac mass measuring 5 × 10 mm attached to the mitral valve leaflet with moderate mitral regurgitation and preserved biventricular function (estimated systolic pulmonary artery pressure 40 mmHg). Based on these findings, a diagnosis of IE was made. Three sets of blood cultures, COVID-19 serology, and immunological testing were obtained. Empirical intravenous vancomycin, gentamicin, and fluconazole were initiated along with anticoagulation after stabilization of bleeding tendency.

Renal Complication

On day 2 of admission, the patient developed acute kidney injury with oliguria, hematuria, and volume overload despite escalated diuretic therapy. Laboratory investigations revealed rising serum urea (133 mg/dL) and creatinine (1.4 mg/dL).

Urine microscopy demonstrated dysmorphic red cells and proteinuria. Complement levels and autoimmune screen were unremarkable. Renal Doppler was normal. The clinical and laboratory profile suggested immune complex–mediated glomerulonephritis secondary to IE. Early bedside peritoneal dialysis was initiated for 48 hours, with subsequent recovery of renal function and improved fluid balance.

Neurological Event

Despite initial stabilization, the patient developed right lower limb weakness on day 11. MRI brain demonstrated a left-sided watershed acute infarction, most likely embolic in origin **(Figure 2)**.

Anticoagulation was continued, and neurology consultation recommended cardiothoracic surgical intervention given the progression of intracardiac mass and embolic complications.

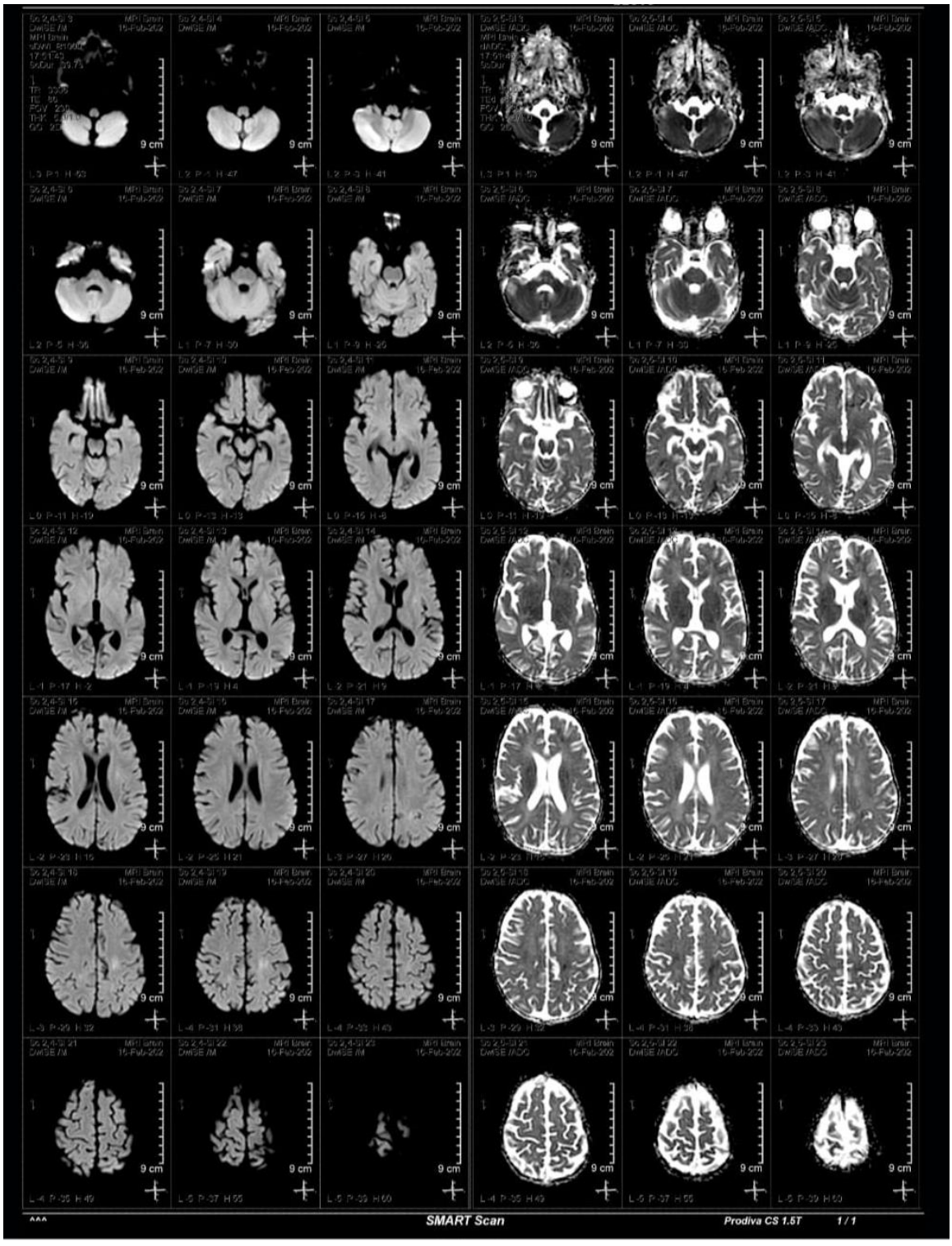

Figure 2: MRI brain showing left-sided infarction

Surgical Management and Outcome

Repeat echocardiography revealed enlargement of the mitral valve mass to 13 × 5 mm, associated with severe mitral regurgitation. The child was transferred to a tertiary center where she underwent surgical removal of the intracardiac thrombus and mitral valve repair without prosthetic replacement. Postoperative echocardiography confirmed complete resolution of the mass with preserved valve function. The patient showed gradual neurological and clinical improvement on follow-up.

A comprehensive summary of the patient's clinical parameters, laboratory investigations, and echocardiographic findings is presented in **Table 1**. This tabulation provides a clear overview of the dynamic changes observed throughout the clinical course, highlighting the progression of systemic inflammation, renal dysfunction, and cardiac involvement.

Table 1: Clinical, laboratory, and echocardiographic parameters of the patient

Parameter	Value	Reference Range
Clinical Parameters		
Mean Arterial Pressure (mmHg)	55	70–100 mmHg
Heart Rate (bpm)	190	80–120 bpm (infant)
Respiratory Rate (cycles/min)	65	20–40 /min (infant)
Temperature (°C)	38.0	36.1–37.2 °C
Oxygen Saturation (room air, %)	88	>95%
Capillary Refill Time (sec)	2	<2 sec
Mechanically Ventilated	Yes	No
FiO_2 (%)	50	<50%
Laboratory Findings		
Hemoglobin (g/dL)	7.4	11–14 g/dL
Mean Corpuscular Volume (fL)	75	76–90 fL
Total Leukocyte Count ($\times 10^9$/L)	7.9	4–12 $\times 10^9$/L
Neutrophils (%)	73	40–60%
Lymphocytes (%)	20	30–50%
Platelets ($\times 10^9$/L)	302	150–400 $\times 10^9$/L
C-Reactive Protein (mg/L)	72	<5 mg/L
Urea (mg/dL)	23 → 133 (peak)	10–40 mg/dL
Creatinine (mg/dL)	0.44 → 1.4 (peak) → 0.5 (recovery)	0.2–0.7 mg/dL (infant)
ALT (U/L)	11	<40 U/L
AST (U/L)	37	<40 U/L
Albumin (g/dL)	4.0	3.5–5.0 g/dL
IL-6 (pg/mL)	18	<7 pg/mL
Procalcitonin (ng/mL)	10.6	<0.5 ng/mL
D-dimer (ng/mL)	5530	<500 ng/mL
Ferritin (ng/mL)	298	12–200 ng/mL
Echocardiographic Findings		
Intracardiac Mass	5 × 10 mm → 13 × 5 mm	Absent
Site of Mass	Attached to mitral leaflet	–
Mitral Regurgitation	Moderate → Severe	None
LVEF (%)	57	≥55%
RV Function	Preserved	Normal
Estimated SPAP (mmHg)	40	<30 mmHg

mmHg: millimeters of mercury, bpm: beats per minute, FiO_2: fraction of inspired oxygen, sec: seconds, g/dL: grams per deciliter, fL: femtoliter, $\times 10^9$/L: $\times 10^9$ per liter, mg/L: milligrams per liter, mg/dL: milligrams per deciliter, U/L: units per liter, g/dL: grams per deciliter, pg/mL: picograms per milliliter, ng/mL: nanograms per milliliter, LVEF: left ventricular ejection fraction, RV: right ventricle, SPAP: systolic pulmonary artery pressure.

Ethical Considerations

This case report was approved by the institutional ethical committee, El Behera Specialized Pediatric Hospital. A written informed consent was obtained from the patient's legal guardians for participation and for the publication of relevant clinical details and imaging, with strict measures taken to preserve confidentiality and privacy. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments governing research involving human subjects.

DISCUSSION

IE in children is a rare but serious condition, with an incidence significantly lower than that in adults[11, 12]. The majority of pediatric cases occur in the setting of CHD, intravascular devices, or chronic comorbidities [11, 13]. Only a minority, estimated at 8–10%, were reported in previously healthy children. Our case illustrates an unusual scenario of culture-negative IE in a 16-month-old female child with no structural heart disease or immunodeficiency, raising the possibility of alternative predisposing factors.

The clinical course in this child was characterized by multiple complications, including immune complex–mediated glomerulonephritis, acute kidney injury requiring peritoneal dialysis, and an embolic ischemic stroke. Renal involvement in IE is well-recognized, most often due to immune complex deposition leading to glomerulonephritis[14-16]. The presence of dysmorphic red cells and proteinuria, in the absence of hemodynamic compromise or vasculopathy, strongly supported this mechanism. Neurological complications, particularly embolic strokes, occur in up to 20–40% of pediatric IE cases and are associated with increased morbidity and mortality[17]. The progressive enlargement of the mitral valve vegetation despite optimal antimicrobial and anticoagulation therapy further underscores the aggressive nature of the disease.

An important feature of this case is the potential contribution of prior SARS-CoV-2 infection. COVID-19 has been associated with endothelial injury, hypercoagulability, and immune dysregulation, which collectively predispose to cardiovascular and thromboembolic events[18]. In children, the post-COVID inflammatory milieu has been most widely described in multisystem inflammatory syndrome in children (MIS-C), but less attention has been given to its role in predisposition to IE[19, 20]. Our patient demonstrated elevated inflammatory and thrombotic markers, including procalcitonin, interleukin-6, ferritin, and markedly elevated D-dimer, suggestive of ongoing immune activation. These findings raise the possibility that post-COVID immune dysregulation created a permissive environment for culture-negative IE in an otherwise healthy child.

Culture-negative endocarditis remains a diagnostic and therapeutic challenge. It accounts for up to 20% of pediatric IE cases and is frequently linked to prior antimicrobial exposure or fastidious organisms such as Coxiella burnetii and Bartonella species, as well as fungi[21, 22]. In our patient, repeated blood cultures were sterile, and serum galactomannan was transiently elevated but normalized, favouring a post-infectious immune state rather than true fungal endocarditis. Empirical broad-spectrum antimicrobial coverage was initiated, and surgical intervention was ultimately required due to progressive vegetation growth and severe mitral regurgitation. Valve repair, rather than replacement, was successfully performed, aligning with pediatric surgical strategies that prioritize preservation of native valves whenever feasible.

This case adds to the growing body of evidence suggesting that COVID-19–related immune dysregulation may predispose children to uncommon and aggressive cardiovascular complications. Early recognition, multidisciplinary management, and timely surgical referral were essential in achieving a favourable outcome.

CONCLUSIONS AND FUTURE PERSPECTIVES

This case highlights a rare occurrence of culture-negative IE in a previously healthy child, complicated by immune complex–mediated glomerulonephritis and embolic stroke, in the context of recent COVID-19 infection. It underscores how post-COVID immune dysregulation and hypercoagulability may predispose children without structural heart disease to aggressive endocardial infections. Favourable outcome was achieved through early recognition, close multidisciplinary collaboration, and timely surgical repair.

Looking ahead, clinicians should maintain high suspicion for endocarditis in children presenting with unexplained systemic inflammation or embolic phenomena following COVID-19, even in the absence of classical risk factors. Future prospective studies and pediatric registries are needed to clarify the pathophysiological links between SARS-CoV-2 infection, immune dysregulation, and endocardial involvement, and to establish standardized diagnostic and management strategies for culture-negative cases in children.

Financial support and sponsorship: Nil.
Conflict of Interest: Nil.

REFERENCES

1. **Gupta S, Sakhuja A, McGrath E *et al.* (2017)**: Trends, microbiology, and outcomes of infective endocarditis in

children during 2000-2010 in the United States. Congenit Heart Dis., 12:196-201.

2. **Mahony M, Lean D, Pham L *et al.* (2021)**: Infective Endocarditis in Children in Queensland, Australia: Epidemiology, Clinical Features and Outcome. Pediatr Infect Dis J., 40:617-22.
3. **Jortveit J, Klcovansky J, Eskedal L *et al.* (2018)**: Endocarditis in children and adolescents with congenital heart defects: a Norwegian nationwide register-based cohort study. Arch Dis Child, 103:670-4.
4. **Ferrieri P, Gewitz M, Gerber M *et al.* (2002)**: Unique features of infective endocarditis in childhood. Pediatrics, 109:931-43.
5. **Carceller A, Lebel M, Larose G *et al.* (2005)**: [New trends in pediatric endocarditis]. An Pediatr (Barc), 63:396-402.
6. **Lin Y, Hsieh K, Chen Y *et al.* (2013)**: Infective endocarditis in children without underlying heart disease. J Microbiol Immunol Infect., 46:121-8.
7. **Baltimore R, Gewitz M, Baddour L *et al.* (2015)**: Infective Endocarditis in Childhood: 2015 Update: A Scientific Statement From the American Heart Association. Circulation, 132:1487-515.
8. **Bigdelian H, Sedighi M, Sabri M *et al.* (2021)**: Case Report: Acute Intracardiac Thrombosis in Children With Coronavirus Disease 2019 (COVID-19). Front Pediatr., 9:656720.
9. **Huang C, Wang Y, Li X *et al.* (2020)**: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 395:497-506.
10. **Guo T, Fan Y, Chen M *et al.* (2020)**: Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol., 5:811-8.
11. **Vicent L, Luna R, Martínez-Sellés M (2022)**: Pediatric Infective Endocarditis: A Literature Review. J Clin Med., 11(11):3217.
12. **Marín-Cruz I, Pedrero-Tomé R, Toral B *et al.* (2024)**: Infective endocarditis in pediatric patients: a decade of insights from a leading Spanish heart surgery reference center. Eur J Pediatr., 183:3905-13.
13. **Snygg-Martin U, Giang K, Dellborg M *et al.* (2021)**: Cumulative Incidence of Infective Endocarditis in Patients with Congenital Heart Disease: A Nationwide, Case-Control Study Over Nine Decades. Clin Infect Dis., 73:1469-75.
14. **Krishnamurthy S, Chandrasekaran V, Mahadevan S *et al.* (2017)**: Severe acute kidney injury in children owing to infective endocarditis-associated immune complex glomerulonephritis: a report of two cases. Paediatr Int Child Health, 37:144-7.
15. **Sayad R, Elsaeidy A, Mokresh M *et al.* (2025)**: Immunosuppressant Use in Infective Endocarditis-Associated Glomerulonephritis: A Systematic Review. Clin Drug Investig., 45:443-529.
16. **Hermanns H, Alberts T, Preckel B *et al.* (2023)**: Perioperative Complications in Infective Endocarditis. Journal of Clinical Medicine, 12:5762.
17. **Rovin H, Adler G, Barratt J *et al.* (2021)**: KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney International, 100:S1-S276.
18. **Jayarangaiah A, Kariyanna P, Chen X *et al.* (2020)**: COVID-19-Associated Coagulopathy: An Exacerbated Immunothrombosis Response. Clin Appl Thromb Hemost., 26:1076029620943293.
19. **ElDefrawy M, Emara AAE-G, Amira., Abdelbaset H (2024)**: Liver Involvement in Children with COVID-19 and Multisystem Inflammatory Syndrome. The Egyptian Journal of Hospital Medicine, 94:34- 41.
20. **Lin J, Harahsheh A, Raghuveer G *et al.* (2023)**: Emerging Insights Into the Pathophysiology of Multisystem Inflammatory Syndrome Associated With COVID-19 in Children. Can J Cardiol., 39:793-802.
21. **Shahani L (2011)**: Culture negative endocarditis: a diagnostic and therapeutic challenge! BMJ Case Rep., 2011:bcr0720114538.
22. **Lin K, Yeh T, Chuang Y *et al.* (2023)**: Blood Culture Negative Endocarditis: A Review of Laboratory Diagnostic Approaches. Int J Gen Med., 16:317-27.